

**MAIL STOP
AMENDMENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: C.C. Lambeth et al. Attorney Docket No.: WEYE115226
Application No.: 09/618,307 Group Art Unit: 1638
Filed: July 18, 2000 Examiner: D.T. Fox
Title: POLLEN POLYMIX PLANT BREEDING METHOD UTILIZING
MOLECULAR PEDIGREE ANALYSIS

RESPONSE TO NON-FINAL OFFICE ACTION

Seattle, Washington 98101

July 20, 2004

TO THE COMMISSIONER FOR PATENTS:

In response to the Office Action mailed April, 20, 2004, please reconsider the application in view of the following comments.

The Examiner is thanked for the courtesy of a telephone interview on June 29, 2004, with applicants' attorneys Barry McGurl and Karen Blöchlinger. The claim rejections were discussed as set forth below, but no agreement was reached regarding allowable subject matter. The Examiner agreed to reconsider the claims in view of the discussion with applicants' attorneys.

Claims 20-31 are pending in the application and have been examined. Claims 20-31 stand rejected. Applicants respectfully request reconsideration and allowance of Claims 20-31.

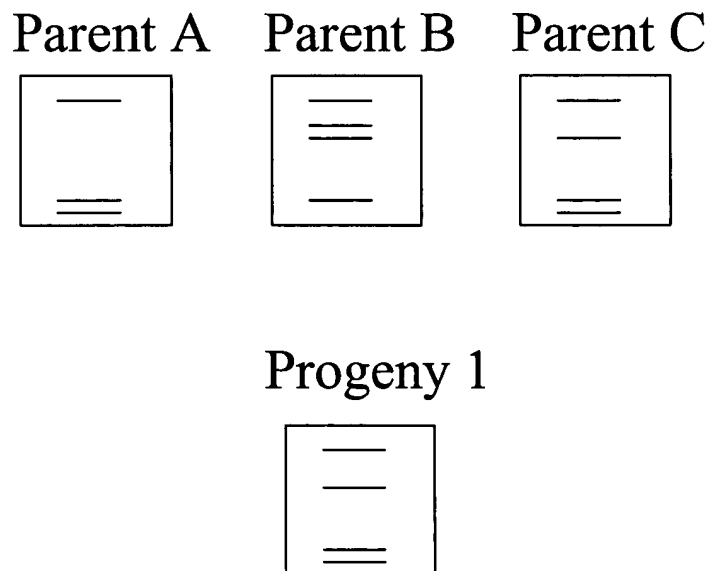
Rejection of Claims 20-31 Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 20-31 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that lacks an adequate written description in the specification. According to the Examiner, the disclosure of SSR markers from a single pine species is not representative of the broadly claimed genus of any type of molecular markers from any taxonomically divergent tree species. The Examiner further states that Staub et al. (1996) *HortScience* 31(5):729-740 supports the Examiner's position in its teaching that marker-assisted selection is still in its

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infancy and is hampered by genetic interactions such as epistasis, loose linkages, and problems in accurate phenotypic classification. Applicants respectfully disagree for the following reasons.

As an initial matter, applicants wish to point out that the claimed invention is directed to a method of tree breeding using DNA analysis to determine the pedigree of progeny trees. The invention is *not* directed to linking DNA markers with one or more phenotypic traits. Instead, DNA analysis is used merely to determine which of the plurality of parental trees represented in the polymix cross gave rise to a specific progeny tree. The DNA analysis step of an exemplary embodiment of the invention in which the pedigree of a progeny plant (progeny 1) from a polymix cross including pollen from three parental plants (parents A, B, and C) is determined using DNA analysis is illustrated in the figure below. The figure shows DNA bands from plants A, B, and C and from progeny plant 1 separated by electrophoresis. Even in the absence of prior knowledge of the sequence and identity of the individual DNA bands, the DNA analysis clearly points to parent C as the parent of progeny 1 because the distribution of bands is the same for parent C and progeny 1.



In contrast, the genetic markers described in Staub et al. are used as "heritable entities that are associated with economically important traits" (Staub et al., page 729, Column 1, first paragraph). In other words, Staub et al. establishes links between markers and specific phenotypic traits, i.e., a specific DNA band is always present in plants that have a particular phenotypic trait, and is absent from plants that do not have the phenotypic trait. The type of analysis practiced by Staub et al. is sometimes referred to as linkage analysis or marker-assisted selection. Often the goal of linkage analysis or marker-assisted selection is to identify a gene that causes a particular phenotypic trait. Because the methods of the invention are not used to link DNA markers with phenotypes, the problems associated with the method of Staub et al. that were alluded to by the Examiner (e.g., epistasis, loose linkages, etc.) are not applicable to the claimed invention.

Moreover, the figure above highlights that a description of all the numerous possible DNA sequences that could be analyzed in the practice of the claimed invention is neither necessary nor feasible. Any DNA sequence polymorphism can be used in the practice of the present invention. A sequence polymorphism can take the form of, for example, an insertion, a deletion, or a single nucleotide change (single nucleotide polymorphism, abbreviated as SNP). Importantly, knowledge of the actual sequence of the DNA marker or its position in the genome is typically not necessary to practice the invention. This point is further illustrated by the following example, in which DNA sequences of a DNA marker in parents A and B are arbitrarily designated to be "ACGGTA" and "ATGGTA," respectively. The sequences "ACGGTA" and "ATGGTA" are unimportant in themselves. What is relevant is that the second nucleotide is polymorphic—that is, it is *different* in these two sequences ("C" in parent A and "T" in parent B)—and that this difference is detectable by one or more methods of DNA analysis (e.g., RFLP, AFLP, sequencing, etc.). A "C" at the second nucleotide position in progeny 1 would indicate

that its parent is parent A, whereas a "T" at the second nucleotide position in progeny 1 would indicate that its parent is parent B. In some embodiments of the invention, this sequence polymorphism causes a difference in size of a DNA fragment that is detectable, for example, by gel electrophoresis, as shown in the figure above. In these embodiments, the pedigree of progeny trees can be determined *without knowing any of the nucleic acid sequence of the DNA marker*. Similarly, if the polymorphism is an insertion or a deletion of one or more nucleotides, the presence or absence of the insertion or deletion can typically be determined indirectly, without knowing the sequence of the relevant polymorphic region (e.g., by observing an increase or a decrease in the size of a band on a gel).

Furthermore, a description of all the possible DNA sequences that could be used in the practice of the claimed invention is impracticable because the number of polymorphisms in any plant species that could be used for the pedigree analysis is enormous. For example, it has been estimated that the maize genome has up to 62 million SNPs (Mogg et al. (1999) Plant and Animal Genome VII Conference Abstract Guide, Sherago International Inc., P491, reviewed in Edwards & Mogg, Plant Genotyping by Analysis of Single Nucleotide Polymorphisms, *in Plant Genotyping: the DNA Fingerprinting of Plants* (ed. R.J. Henry, 2001), page 3, submitted in a Supplemental Information Disclosure Statement filed concurrently herewith). This estimate illustrates that it would not be realistic to provide a written description of every possible polymorphism in the genome of every tree species.

In addition, applicants submit that a requirement for a written description for every possible DNA sequence useful for pedigree analysis in trees would not further the policy of providing public notice of the boundaries of the claimed invention in this case. One of skill in the art would clearly be apprised that the claims encompass any form of DNA analysis to determine the pedigree of progeny plants.

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For the reasons described above, and in responses filed on June 2, 2003 and January 27, 2004, applicants submit that Claims 20-31 are supported by an adequate written description and respectfully request removal of this ground of rejection.

The Rejection of Claims 20-31 Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 20-31 stand rejected under 35 U.S.C. Section 112, first paragraph, for lack of an enabling description in the specification. The Examiner states that the isolation of DNA markers is not the issue but that Staub et al., White (1996) *Proc. QFRI-IUFRO Conf. Tree Improvement for Sustainable Tropical Forestry*, p. 110-117, and Lambeth et al. (2001) *Theor. Appl. Genet* 103: 930-943 demonstrate the unpredictability inherent in the claimed process. Applicant respectfully disagrees with the Examiner's conclusions for the following reasons.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in a patent coupled with information known in the art at the time of filing without undue experimentation. Not everything necessary to practice the invention need be disclosed: according to the Federal Circuit, "a patentee preferably omits from the disclosure any routine technology that is well known at the time of application." *Chiron v. Genentech*, 70 U.S.P.Q.2d 1321, 1325 (Fed. Cir. 2004). The Federal Circuit has explained:

That is not to say that the specification itself must necessarily describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments, depending upon the predictability of the art. *Chiron v. Genentech*, 70 U.S.P.Q.2d 1321, 1325 (Fed. Cir. 2004) (citing *AK Steel Corp. v. Sollac*, 68 U.S.P.Q.2d 1280 (Fed. Cir. 2003)).

The Examiner states that Staub et al. shows the unpredictability of marker-assisted selection. As described in the preceding section, applicants' invention is not directed to marker-assisted selection but to a tree breeding method using DNA analysis to establish the pedigree of

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progeny trees obtained from a polymix cross. Thus, Staub et al. does not show that a tree breeding method using DNA analysis to establish the pedigree of progeny trees is unpredictable.

The Examiner states that White teaches that open pollination is unpredictable. However, applicants' invention is not directed to a breeding method using open pollination (*i.e.*, a pollination method in which a tree can be pollinated with pollen from any source). Instead, applicants' inventive method uses polymix breeding in which a mixture of pollen obtained from a defined breeding group of trees is used to pollinate a defined group of trees.

The Examiner states that the failures observed in Lambeth et al. shows that the process is unpredictable. As an initial matter, Lambeth et al. is a publication by the inventors describing one of the embodiments of the invention. It does not constitute prior art because it was published after the filing date of the present application.

According to the Examiner, Lambeth et al. admit that the success observed by them was dependent on a particular breeding population and a small number of markers. Applicants respectfully disagree. First, Lambeth et al. describes 3 cases out of 45 in which the observed genotypes were not consistent with the expected genotypes. Rather than showing that the process is unpredictable, these results indicate that in more than 93% of cases the expected result was obtained. Second, Lambeth et al. attribute the *failures* rather than the *successes* to the breeding population—specifically, the considerable relatedness of the breeding population—and the small number of markers used (Lambeth et al., Abstract). Moreover, Lambeth et al. point out that these inconsistencies could have arisen due to an inaccurately labeled pedigree, which is known to occur with a higher than acceptable frequency in tree breeding and which could be avoided by the routine use of markers in confirming parentage in progeny tests (Lambeth et al., page 936, Column 2). Finally, Lambeth et al. note that "[t]he inclusion of more markers and/or the creation of polymixes and breeding groups that avoid relatedness would resolve this

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problem" (Lambeth et al., Abstract; see also Specification, page 19, line 30, to page 20, line 2). Therefore, Lambeth et al. does not support the Examiner's conclusion that the claimed process is unpredictable.

Applicants respectfully submit that, as fully described in applicants' response filed on January 27, 2004, the specification contains specific guidance on the identification of genetic polymorphisms from a variety of tree species to enable the determination of the pedigree of progeny trees by DNA analysis. In addition, numerous other genetic polymorphisms in trees were well known in the art at the time of filing this application for many tree species, as shown in the publications attached to applicants' response filed on January 27, 2004. Since these publications did not reach the Examiner, they are herewith being submitted in a Supplementary Information Disclosure Statement, as requested by the Examiner.

For the reasons described above, and in those described in response to the Office Actions mailed January 2, 2003 and August 27, 2003, applicants submit that Claims 20-31 are supported by an enabling description and respectfully request removal of this ground of rejection.

The Rejection of Claims 20-31 Under 35 U.S.C. § 103(a)

Claims 20-31 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Bridgwater (1992) in *Handbook of Quantitative Forest Genetics*, Kluwer Academic Pub., Dordrecht, The Netherlands, pages 69-95 in view of El-Kassaby & Ritland (1992) *Theor. Appl. Genet.* 83(6-7):752-8 and Stoehr et al. (1998) *Can. J. For. Res.* 28: 187-95. According to the Examiner, it would have been obvious to one of ordinary skill in the art to utilize the method of polymix tree breeding taught by Bridgwater, and to modify that method by utilizing the pedigree analysis step in the Douglas fir polymix breeding program taught by El-Kassaby & Ritland and to further modify that method by utilizing the DNA marker taught by Stoehr et al.

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For the reasons set forth in detail below, applicants respectfully submit that the burden of establishing a *prima facie* case of obviousness has not been met because there is no suggestion to combine or modify the reference's teachings to arrive at the claimed invention. The claimed invention is directed to a method for tree breeding. Claim 20, from which Claims 21-31 depend, recites the following steps:

- (a) mixing pollen obtained from a breeding group comprising a plurality of parental trees to obtain a pollen polymix;
- (b) pollinating female reproductive structures from each parental tree in the plurality of parental trees with the pollen polymix to obtain a plurality of progeny lots, wherein each progeny lot comprises seeds obtained from a different cross between the pollen polymix and each different parental tree of the plurality of parental trees;
- (c) evaluating progeny trees grown from each of the progeny lots using objective criteria to obtain a phenotype score;
- (d) determining the pedigree of a plurality of progeny trees using DNA analysis; and
- (e) using the pedigree and phenotype score to identify elite trees for use in a next generation of tree breeding.

Applicants respectfully submit that Bridgwater does not teach or suggest step (d) determining the pedigree of a plurality of progeny trees using DNA analysis or step (e) using the pedigree and phenotype score to identify elite trees for use in a next generation of tree breeding, as required by Claim 20. Instead Bridgwater simply provides a review of different types of mating designs used in breeding programs, including polymix breeding. Bridgwater provides no suggestion or motivation to either use DNA analysis to determine the pedigree of progeny trees, as recited in step (d) of the claimed method, or to use a pedigree and a phenotype score to identify elite trees, as recited in step (e) of the claimed method. As further described below, neither El-Kassaby & Ritland nor Stoehr et al. provide any motivation or suggestion to modify the teachings of Bridgwater to arrive at the claimed invention.

Applicants submit that El-Kassaby & Ritland does not teach or suggest any of the steps of (c) evaluating progeny trees grown from each of the progeny lots using objective criteria to obtain a phenotype score, (d) determining the pedigree of a plurality of progeny trees using DNA analysis, or (e) using the pedigree and phenotype score to identify elite trees for use in a next generation of tree breeding, as required by Claim 20. El-Kassaby & Ritland describes a study of male reproductive success using a polymix of three pollen donors, in which the paternity of progeny was determined based on four protein markers. El-Kassaby & Ritland provide no suggestion or motivation to use their method of determining paternity in a tree breeding program. Specifically, there is no suggestion or motivation in El-Kassaby & Ritland to determine the pedigree of progeny trees using DNA analysis and using the pedigree information as well as a phenotype score to identify elite trees.

Similarly, applicants submit that Stoeher et al. does not teach or suggest the steps of (c) evaluating progeny trees grown from each of the progeny lots using objective criteria to obtain a phenotype score or (e) using the pedigree and phenotype score to identify elite trees for use in a next generation of tree breeding, as required by Claim 20. Rather, Stoeher et al. used a polymorphic genome marker to estimate the level of outside-orchard pollen contamination, supplemental mass pollination efficacies and natural selfing in Douglas fir (Stoeher et al., Abstract). Stoeher et al. provides no motivation or suggestion to use their method in a tree breeding program. Specifically, there is no suggestion or motivation in El-Kassaby & Ritland to use pedigree information as well as a phenotype score to identify elite trees.

Therefore, none of the references cited by the Examiner, alone or in combination teach or suggest the steps of the claimed invention. In particular, none of the references teach or suggest the step of (e) using the pedigree and phenotype score to identify elite trees for use in a next generation of tree breeding. For the reasons noted above, the cited references fail to teach,

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suggest, provide any motivation to make or otherwise render obvious the claimed invention. Accordingly, applicants respectfully request withdrawal of this ground of rejection.

Supplemental Information Disclosure Statement

The Examiner noted he did not receive the references appended to the response submitted on January 30, 2004. As suggested by the Examiner, these references, as well as those cited in this response, are being submitted in a Fourth Supplemental Information Disclosure Statement filed concurrently herewith. The Examiner is respectfully requested to reconsider applicants' arguments set forth in the amendment dated January 27, 2004, in view of the attached references.

CONCLUSION

In view of the foregoing remarks, applicants respectfully submit that all the pending claims are in condition for allowance. If any issues remain that may be expeditiously addressed in a telephone interview, the Examiner is encouraged to telephone applicant's attorney.

Respectfully submitted,

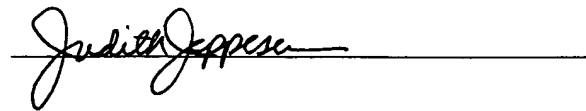
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